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HIGHLIGHTS

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Sequenom to Petition U.S. Supreme Court to Regain MaterniT21 Test Patent

With its sales and margins suffering unrelenting pressure, the beleaguered molecular testing firm Sequenom has decided to petition the United States Supreme Court in an attempt to regain a patent for a genetic test it lost three years ago.

The petition is centered on what has been referred to in laboratory circles as the "540 patent," in reference to the last three numbers of a patent Sequenom held until 2013 that it applied to its MaterniT21 test. That assay is used to analyze cell-free fetal DNA in a mother's blood to diagnose genetic conditions.

The U.S. Supreme Court invalidated two patents held by Prometheus Laboratories. Those patents, which used metabolite levels in the blood-

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Mayo Clinic to Shut Down New England Laboratory

The Mayo Clinic is pulling back on its laboratory operations in the Eastern U.S. The hospital system's for-profit Mayo Clinic Laboratories subsidiary will shut down its laboratory in Andover, Mass. by the end of this year, officials said. The operations of Mayo Medical Laboratories New England will be transferred to Rochester, Minn., where the Mayo Clinic is headquartered, in phases throughout this calendar year.

The Mayo Clinic entered the East Coast market with the acquisition of New England Pathology Services in the 1990s. However, it became clear to the legendary health care provider that the Massachusetts lab had become disconnected from the rest of its clinical operations. Its long-term lease for the facility was expiring, and Mayo management decided they did not wish to renew for another decade.

Quest Diagnostics also recently opened a massive 200,000 square-foot laboratory in nearby Marlborough, Mass.,—the result in part of its 2012 acquisition of the outreach business of the University of Massachusetts Memorial Medical Center. That likely is making the

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■ Mayo Clinic to Shut Down New England Laboratory, *from page 1*

competitive environment for lab services in Central Massachusetts extraordinarily fierce. Quest also briefly hired Mayo Lab's former CEO in the autumn of 2014 as its chief laboratory officer, although he resigned his new position after Mayo sued.

> *"The initial focus of the laboratory was supporting (Mayo's) now-discontinued clinical trials testing service line, but the test menu has evolved into locally performed high-volume tests from our clients in the Northeast."*
>
> — Gina Chiri-Osmond

"This testing facility is a highly successful operation in terms of quality, safety, productivity, and cost efficiency," said William Morice, M.D., chair of Mayo's pathology and laboratory medicine departments, in a statement. "However, the facility is not near a Mayo Clinic medical practice. Our decision is based upon the long-term future for this facility, not the great work that is performed here every day."

With high margin molecular testing being performed in Minnesota, the New England laboratory primarily performed toxicology, microbiology, immunology and vitamin deficiency testing. It offers a menu of about 400 assays in total. That's a fraction of the 3,000 or so tests and pathology procedures Mayo Clinic Laboratories offers in total. The laboratory division has also entered into deals with a variety of esoteric laboratories to offer their tests to patients.

"The initial focus of the laboratory was supporting (Mayo's) now-discontinued clinical trials testing service line, but the test menu has evolved into locally performed high-volume tests from our clients in the Northeast," said Mayo Clinic spokesperson Gina Chiri-Osmond.

Chiri-Osmond declined to say what the monthly testing volume was, or how it has changed over the years. It had developed a significant outreach business, but no specifics on that were available.

Altogether, the laboratory employs 105 people. All of them may keep their jobs if they are willing to relocate.

"Our hope is that all of the staff would want to continue their careers at other Mayo locations (the system has facilities in Florida, and Arizona as well as Minnesota, with a laboratory facility in Jacksonville, Fla.). We would offer relocation packages for them," Chiri-Osmond said. "However, for those who choose not to stay with Mayo, we are offering severance packages based on their length of service with Mayo."

Takeaway: The Mayo Clinic is rolling back and consolidating a portion of its wide-ranging laboratory operations. G2

FDA Intervenes on Development of New Zika Test

The health care sector may have developed a rapid detection diagnostic test for the Zika virus, but the U.S. Food and Drug Administration (FDA) may wind up intervening prior to it making a significant impact.

The test was developed jointly by pathologists and researchers at Texas Children's Hospital in Houston and Houston Methodist Hospital. The two providers announced it in late February.

The Zika virus has become a low-level pandemic in recent months. The virus initially spreads through mosquitoes, but it can also be sexually transmitted from men to women. Although the virus itself causes relatively mild symptoms in adults, children of mothers infected can be born with serious birth defects, including microcephaly. Brazil has been struggling with an outbreak of Zika-related microcephaly since the middle of last year. According to data from the U.S. Centers for Disease Control and Prevention, there were 273 confirmed domestic cases of Zika, all related to overseas travel. Of those, 19 are in pregnant women. Another 286 cases have been reported in U.S. territories, with most of them acquired locally.

"With travel-associated cases of the Zika virus becoming more prevalent in the United States, coupled with the looming increase in mosquito exposure during spring and summer months, we must be prepared for a surge of Zika testing demand."

— James Versalovic, M.D.

"With travel-associated cases of the Zika virus becoming more prevalent in the United States, coupled with the looming increase in mosquito exposure during spring and summer months, we must be prepared for a surge of Zika testing demand," said James Versalovic, M.D., chief pathologist at Texas Children's Hospital. "We must provide answers for anxious moms-to-be and families who may experience signs and symptoms or may simply have travel history to endemic areas."

The test, which focuses on RNA analysis, can be deployed using blood, amniotic fluid, urine or spinal fluid. Turnaround is a few hours, officials said.

Days after the hospitals made the joint announcement, the FDA sent an "it has come to our attention letter" to Versalovic and James Musser, M.D., a pathology professor connected with Houston Methodist.

"We believe that due to the current public health emergency it is appropriate for the Food and Drug Administration to review information related to the development of the test," the letter said. "Based on our review of your promotional materials, we believe you are offering a high risk test that has not been the subject of premarket clearance, approval, or emergency use authorization review by the FDA. The FDA would like to better understand the test's design, validation and performance characteristics, and in addition, CDC and CMS have asked us to review the science behind your test."

There is currently only one test for Zika approved by the FDA for commercial use on an emergency basis. That test, developed by the CDC, focuses on antibodies and is not 100 percent accurate.

The FDA's questioning about the test is likely being spurred over a clash with the sector over its proposed regulation of laboratory developed tests. The agency claims that many assays, due to their complexity and touted diagnostic powers, could pose dangers to patients if they are not properly regulated. Last year, the FDA released a remarkable report listing 20 current and former lab tests it claimed were potentially dangerous.

Laboratory leaders have fiercely resisted the proposal, saying that relatively minor changes to CLIA regulations would suffice. The FDA has yet to issue final guidelines. A spokesperson for Texas Children's Hospital and Houston Methodist Hospital did not respond to a query seeking comment.

Takeaway: The Food and Drug Administration may intervene in the distribution of any laboratory developed tests related to the Zika virus. G2

Inside The Lab Industry

A Slow But Growing Push for Greener Laboratories

Ilyssa Gordon, M.D., is a gastrointestinal pathologist by profession and an environmentalist by passion.

When she joined the staff of the Cleveland Clinic four years ago, she decided to delve into the guts of its wide-ranging hospital laboratory operations, trying to determine how it could be greener and therefore more efficient—both operationally and fiscally.

These days, there are a lot of questions laboratory directors can ask regarding more environmentally friendly practices and operations, observers and experts say.

The Cleveland Clinic had actually opened a new main hospital lab about a year before Gordon was hired on, a state-of-the-art facility that boasted a certification from the Leadership in Energy and Environmental Design, or LEED. But that honorific was primarily due to the lab's construction, not necessarily its day-to-day operations.

"I met with my institute chair, and got permission to look around and ask questions," Gordon recalled.

These days, there are a lot of questions laboratory directors can ask regarding more environmentally friendly practices and operations, observers and experts say. Even as the sector moves on toward more high-tech testing that relies on digital imaging and embraces practices such as recycling, there remain many areas where greener practices may be adopted.

For example, many labs still use mercury-based stains and fixatives—although there are many mercury-free alternatives that work just as well. Many labs do not reprocess widely-used solvents such as alcohol and formalin, instead paying outside firms to cart it away and dispose of it. And traditional recycling for paper and plastic often omits huge amounts of material. There are also extensive opportunities for cutting down on ventilation costs, although CLIA regulations contain air flow mandates that do not apply to non-medical research laboratories.

"There is great work being done in hospital laboratories around the country," said Cecilia DeLoach Lynn, director of sector performance with Practice Greenhealth, a Virginia-based trade group that encourages more environmentally-friendly practices among hospitals and other health care providers. And while data is currently lacking in many areas, cost savings appear to be considerable for even small measures.

According to Lynn, a group of as many as 220 hospital laboratories that chose to reprocess their solvents saved more than $639,000 over the course of a year, along with ensuring that 39,000 gallons of hazardous waste did not wind up in

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a disposal site. Albany Medical Center in upstate New York invested $150,000 in the mid-1990s in a solvent reprocessing system and has saved more than $2 million since.

Recycling—But Not Recycling

One of the things Gordon quickly discovered within the Cleveland Clinic lab system is that while recycling of many paper and plastic items was taking place, literally tons of material was falling through the cracks. Cardboard, paper and hard plastics were being recycled, but materials such as styrofoam and soft plastics were not. That meant plastic wrappers, bubble wrap and paperboard containers for items such as gloves—were being thrown out with conventional garbage.

The Cleveland Clinic's labs gathered up a week of potentially recyclable waste for a greening campaign. The amounts were massive, Gordon said. It contracted with a non-profit firm to sort and recycle those items moving forward.

Another issue was the myriad biohazard safety cabinets within the Cleveland Clinic's labs. Oftentimes, the sashes to the cabinets were being left open on an ongoing basis, meaning their ventilation systems were running non-stop. That practice was modified to keep the ventilation running only when the cabinets were in use.

According to Daniel Doyle, Chief Executive Officer of Grumman/Butkus Associates, a Chicago-area design engineer firm that specializes in the health care sector, ventilation can account for as much as 80 percent of all electricity usage.

Ventilation systems are one of the biggest keys to saving energy and cutting costs in a laboratory space. According to Daniel Doyle, Chief Executive Officer of Grumman/Butkus Associates, a Chicago-area design engineer firm that specializes in the health care sector, ventilation can account for as much as 80 percent of all electricity usage.

However, medical laboratories are constrained compared to research laboratories in terms of the changes they can make. "Clinical labs tend to be smaller (than research labs), and more heavily regulated by state codes and (accreditation bodies such as the) Joint Commission. That means there tends to be less opportunity for making big changes," Doyle noted. He added that in Illinois, for example, clinical laboratories are required to have a near constant airflow in work spaces.

Nevertheless, labs can still design HVAC systems that can recover up to 65 percent of the heat being expended, Doyle said. For labs in cold winter climates such as the upper Midwest, that can generate considerable savings on an annual basis.

A study by the organization Laboratories for the 21st Century concluded that such systems can cut space heating and reheating for dehumidification by more than 35 percent, no matter the climate. Fox Chase Cancer Center in Philadelphia invested

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about $300,000 in system modifications and expects to recoup the cost in about four years, according to the study.

Labs also have more options on freezer systems, which have become vastly more efficient in recent years. And newer autoclave systems often also use far less water than their older counterparts. In jurisdictions where such systems are permitted, water running through a continuous loop to cool equipment or for other uses can also be far more efficient and thrifty, according to Doyle.

Steps Toward A Greener Laboratory

- Usage of LED lighting systems that require less electricity and give off less heat than older modes of lighting
- Recycling of all plastics and papers, including styrofoam and device packaging that may not fit within traditional recycling guidelines
- Reprocessing and reuse of solvents such as xylene, alcohols and formalin
- Reduction of biological waste to harmless forms instead of its incineration
- Replacement of mercury-based stains and fixatives with mercury-free alternatives
- Reformatting HVAC systems to be more energy efficient, including recapturing heat from water-cooled equipment; recapturing refrigerants such as Freon, and placing some non-workbench space outside of the laboratory area where CLIA mandates on ventilation do not apply
- Deploying water recovery systems
- Systematic recycling of batteries used in the lab
- Systematic recycling of obsolete analyzers, devices and computers

Sources: Practice Greenhealth, Laboratories For The 21st Century, U.S. Department of Health and Human Services

Cost Savings Not Yet Being Closely Calculated

But how much thriftier a greener laboratory can be is still being quantified, according to Gordon. There are some case studies out there such as the solvent reprocessing data, but it remains patchy. As Practice Greenhealth focuses more on hospital laboratories and other lab operations, the cost savings and return on investments should come into clearer focus.

That will prove crucial for what Gordon believes is one of the most important steps: obtaining buy-in from senior management.

"In a research lab, the buy-in is bottom-up. In a hospital lab, it's top-down," she said, adding that purchasing decisions in that environment are made by senior management. Gordon also acknowledged that the clout of a medical staff member such as herself made it easier to enact changes.

But that's not to say that staff at any level can't successfully promote a green agenda, particularly if the entire system is dedicated to improving the environmental performance of the lab or entire institute. "Anybody can do it," Gordon said.

Takeaway: The laboratory sector is slowly but surely moving toward more environmentally friendly practices that could eventually help their bottom lines. G2

Sequenom to Petition U.S. Supreme Court to Regain MaterniT21 Test Patent, *from page 1*

stream to guide the dosage levels of certain drugs, merely described a law of nature and a "well-understood, routine, conventional activity."

The rationale in that case was applied by the courts the following year to invalidate patenting of the use of cell-free fetal DNA for genetic profiling, as its presence was considered to be naturally occurring.

"We continue to believe that the groundbreaking techniques embodied in the '540 patent' are eligible for patent protection."

— Dirk van den Boom, CEO, Sequenom

The San Diego-based Sequenom lost at both the district court and appellate court level, with the appellate judges saying last December that they were bound by the Prometheus decision. However, one dissenting judge, Pauline Newman, an appointee of President Ronald Reagan, observed that "the new diagnostic method here is novel and unforeseen, and is of profound public benefit." Judge Richard Linn, an appointee of President Bill Clinton, said he only went along with the majority because of the sweep of the Prometheus case, suggesting that some guidance as to how it should be applied in the future may be in order.

As a result, Sequenom is essentially asking the High Court to narrow the scenarios in which the rationale from Prometheus may be applied.

"We continue to believe that the groundbreaking techniques embodied in the '540 patent' are eligible for patent protection," said Sequenom Chief Executive Officer Dirk van den Boom, in a statement. "More broadly, we believe our case provides a compelling opportunity for the Supreme Court to clarify patent eligibility criteria to protect the significant investments made by Sequenom and other life science organizations that have undoubtedly advanced the standard of patient care and treatment, as well as encouraging future such investments."

Whether or not the Supreme Court would take the case remains to be seen; it only grants hearings for a tiny minority of petitions that are presented. A 2013 case it decided, *Association for Molecular Pathology v. Myriad Genetics*, invalidated a patent Myriad tested for the BRCA gene, suggesting that it is likely to hew to a fairly narrow path as to what kind of testing is patentable. As a result of the Myriad case, BRCA testing's price dropped from about $4,000 to less than $1,000 as other laboratories began offering similar assays. Myriad initially reported a drop in revenue, but has since made it up with other testing lines.

In calendar 2013, Sequenom had reported a nearly tripling of revenue from 2012 to $119.6 million. Revenue reached $148.6 million in 2014 and Sequenom broke into the black. Last year, revenue declined to $119.8 million while the company reported a loss of $16.3 million.

In January, Sequenom announced a restructuring that included the planned divestment of its laboratory in North Carolina. The company's stock price, which in 2008 traded for more than $26 a share, has dropped by two-thirds in the past 10 months to about $1.50 a share in recent trading.

Takeaway: Under significant financial pressure, Sequenom is taking a last-ditch approach with the U.S. Supreme Court in an attempt to gain more market control over its cell-free fetal DNA assays. G2

INDUSTRY BUZZ

Patient Age Can Impact Gene Expression

A new study commissioned by the Provista Diagnostics molecular laboratory has concluded that the age of patients can play a role in the expression of genes. Specifically, the study addressed tumor-associated antibodies, which are generated based on the specific kind of cancer that has developed.

"The data allows us to produce blood-based tests to provide accurate results regardless of age."

— Susan Gross, M.D., CMO, Provista

The New York City-based Provista studied the antibodies and serum protein bio-markers of 492 women between the ages of 25 and 75 who received either a benign or suspicious assessment from diagnostic imaging. There were age-related differences found in the majority of individual protein biomarkers even when accounting for breast density and cancer prevalence.

Specifically, after the age of 50, patients are at higher risk for tumor-associated antibodies to undergo significant changes. The alterations are believed to be associated with hormone changes associated with menopause.

"The data allows us to produce blood-based tests to provide accurate results regardless of age," said Susan Gross, M.D., Provista's chief medical officer. The findings were presented at the recent Miami Breast Cancer Conference. They have not yet been published in a peer-reviewed journal.

"While there have been studies showing age being a factor in serum protein biomarker expression, we believe this is the first study to examine whether there were age-related differences in the expression of tumor-associated antibodies" said lead investigator Kasey Benson of Provista in a statement. "These results show that there are differences in the (expression of these antibodies) and this knowledge is extremely valuable."

Provista has been using the data to guide the development of its Videssa breast assay. That test, which is designed to detect breast cancer in patients with dense breasts or inconclusive mammography studies, is expected to be released later this year. The Videssa assay has also been designed to test for ovarian and endometrial cancers.

Provista received $5.25 million in funding from investors last month, and another $6 million last September. It has received a total of nearly $38 million in capital since 2011.

Takeaway: Provista Diagnostics' research has shown an age differential for molecular testing results, which could guide treatments in the future. G2

References

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